REMARKS

The Office Action has withdrawn from consideration Claims 85-102, alleging that the subject matter therein is patentably distinct from the subject matter being prosecuted in the present application. In addition, the Office Action has objected to Claim 82. Further, the Office Action has rejected Claims 35, 36, 40-49, 57, and 68-84 under 35 U.S.C. §112, first paragraph, as allegedly being non-enabling. Furthermore, it has rejected Claims 35, 36, 40-49, 57 and 68-84 under 35 U.S.C. §112, second paragraph, as allegedly failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Finally, Claims 35, 36, 40-49, 57, and 68-84 are rejected under 35 U.S.C. §103 as defining subject matter which is allegedly rendered obvious by the teachings in U.S. Patent No. 5,378,729 to Kohn et al ("Kohn et al.") in view of an article by Post, et al., in Psychopharmacology 1996, 128, 115-129 ("Post et al.") or an article by Yang et al. in Psychiatry and Clinical Neurosciences, 1998, 52 (4), 429-431 ("Yang et al.") or an article by Keck, et al in J. Neuropsychol and Clinical Neurosciences, 1992, 4, 395-405 ("Keck et al.").

Applicant has amended the claims, cancelled others and added claims which, when considered with the Declaration of Robert H. Harris, Ph.D. and the comments hereinbelow, are deemed to place the present case in condition for allowance. Favorable action is respectfully requested.

At the outset, before addressing the merits of the issues raised in the Office Action, applicant wishes to thank Examiner Lukton for the courtesy extended to his representative during the telephone interview on November 15, 2005, and for his helpful suggestions.

Moreover, it is to be noted that the applicant has amended the claims. Claims 35 and 82 have been amended to correct grammatical error therein. In addition, to be consistent with the terminology used in the present application, applicant has amended the term "bipolar disease" to "bipolar disorder" in Claim 35. Applicant has also amended Claims 40-43 by inserting the term "said" therein.

Applicant has also added Claims 103-120 to the application. Support for these added Claims is found on page 20, line 1 to page 23, line 23 and page 24, line 3 to page 27, line 10 of the instant application.

The amendments to the claims also delete subject matter. Applicant has not abandoned this subject matter and reserve the right to file a continuation application directed thereto.

No new matter is added to the application.

Applicant has cancelled Claims 85-102 without prejudice. Nevertheless, applicant reserves the right to file a divisional application directed to the subject matter therein.

Although not stated in this Official Action, it is assumed that the Office Action is alleging that the subject matter in Claims 85-102 is directed to a patentably distinct invention and is implicitly referring to the Restriction Requirement imposed in the underlying application of U.S. Patent No. 6,884,910. Applicant reiterates the rationale therein in its Response to the Restriction Requirement therein which is incorporated herein by reference.

It is to be understood that the cancellation of Claims 85-102 is not considered an acquiescence of the Office Action's Restriction Requirement.

Applicant's amendment to Claim 82, where the spelling of the word "is" is corrected, overcomes the objection thereto. Withdrawal thereof is respectfully requested.

Pursuant to the rejection of Claims 35, 36, 40-49, 57, and 68-84 under 35 U.S.C. §112, first paragraph, the Office Action alleges that it does not believe that the claimed subject matter has the alleged utility. However, the Office Action has improperly placed the burden on applicant to show that the compounds of the present invention are enabled for the treatment of bipolar disorder.

Applicant respectfully submits that the United States Patent and Trademark Office has not met its burden establishing that the application is non-enabling. In order to make a proper rejection, the Office Action has the initial burden to establish a reasonable basis to question the enablement for the claimed invention. In re Wright, 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1515 (Fed. Cir. 1993). Case law has held that the specification disclosure, which contains a teaching of the manner and process of making and using an invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented must be taken as being in compliance with the enablement requirement of 35 U.S.C. §112, first paragraph, unless there is a reason to doubt the objective truth of the statements contained therein which must be relied on for an enabling support. In re Marzocchi, 439 F.2d 220, 224, 169 USPQ 367, 370 (CCPA 1971). As stated by the Marzocchi Court, "it is incumbent upon the Patent Office, whenever a rejection on this basis is made, to explain why it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement. Otherwise, there would be no need for the applicant to go to the trouble and expense of supporting his presumptively accurate disclosure." 439 F.2d at 224, 169 USPQ at 370.

The present application discloses that the compounds described therein are useful for treating bipolar disorder. The Office Action has not provided any evidence that contradicts

the teachings therein. It makes mere conclusions, such as on Page 4 of the Office Action where it states that "[a]t this stage, the most important point is to observe that the 'state of the art' is such that the skilled psychiatrist or neurologist would have no reason to expect that compounds which induce analgesia will be effective to treat bipolar disorder". However, it has presented no evidence which specifically suggests that the compounds of the present invention are not effective in treating bipolar disorder. It provides no data which contradicts the applicant's assertion that the compounds described in the present invention can be used to treat bipolar disorder. It provides no references which shows that the compounds of the present invention cannot be used to treat bipolar disorder.

It does, however, present an article by Singh, in Psychiatr. Clin. N. Am. 2005 28, 301, previously provided by Applicant, which shows that some anticonvulsants are not effective in the treatment of bipolar disorder. But, the compounds therein are so structurally unrelated to the compounds described in the present invention, that the teachings therein provide no insight as to whether the compounds of the present invention have the requisite utility.

The Office Action has indicated that there are no working examples which show the skilled artisan how to use the compounds to treat bipolar disorder. However, case law has held that working examples are not necessary if the application provides sufficient teaching for one of ordinary skill in the art to make and use the invention without an undue amount of experimentation. In re Borkowski, 422 F.2d 904, 908, 164 USPQ 642, 645 (CCPA 1970).

The present application provides such a teaching. Attention is this matter is directed to Page 43, lines 9-21 of the instant specification, which indicate that the treatment regimen is determined by the physician and that the dosage level is generally the same as comparable therapeutic agents. The application also describes different modes of administration

of the compound of the present invention. See, for example, discussions on Page 43, Line 7 to Page 48, Line 14. Moreover, attention is directed to Page 52, lines 30-32 of the instant specification, which exemplifies and incorporates the discussion on Page 43 et seq which describes the amount of drug to be administered for therapeutic effects. Based on the teachings therein, one of ordinary skill in the art is provided sufficient information to use the compounds described in the instant application for treating bipolar disorder without an undue amount of experimentation.

Thus, the United States Patent and Trademark Office has not provided a reasonable basis to question the enablement of the claimed invention.

In addition, applicant is enclosing herewith a Declaration by Dr. Robert Harris ("Declaration") which supports the allegations in the instant specification that the compounds described therein are useful for the treatment of bipolar disorder. Although the Declaration is unexecuted, the contents thereof have been approved by the declarant. An executed copy of the Declaration will be submitted in due course.

In the Declaration, Dr. Harris discusses the test results of two representative compounds of the present invention, viz, 2R-2(acetylamino)-N-[(3-flurophenyl) methyl]-3-methoxypropionamide, designated as Compound 1, and 2-(acetylamino)-2-methoxyamino)-N-benzylacetamide, designated as Compound 2. Compound 1 was subjected to an in vitro test that predicts whether a particular drug is useful for treating bipolar disorder. As described in the Declaration, the set of experiments conducted with Compound 1 are based on an assay which shows a common effect on neurons of three widely prescribed drugs (lithium, valproic acid, and carbamazepine) used for the treatment of bipolar disorder. See ¶9 of Declaration. As testified by Dr. Harris, this assay is sensitive enough to distinguish between those drugs which are used to

treat bipolar disorder and those that are not normally used to treat bipolar disorder. See ¶9-10 of Declaration. The results described in the Declaration show that the representative compound of the present invention behaves like lithium and valproic acid and exhibits mood stabilizing activity for the treatment of bipolar disorder. See ¶11-13 of Declaration. Thus, based thereon, it is concluded that Compound 1 is useful for the treatment of bipolar disorder. See ¶16 of Declaration.

Compound 2, also a representative compound of the present invention, was subjected to testing in an in vivo animal model that responds to lithium, a drug utilized for the current treatment of bipolar disorder. The results show that the representative compound behaved similarly to lithium in this test by antagonizing amphetamine-induced hyperactivity, just like lithium. See ¶20-24 of Declaration. Since the representative compound behaves like lithium in this animal model, and since lithium is used to treat bipolar disorder, one can conclude that the compounds of the present invention are useful in treating bipolar disorder. See ¶23 of Declaration. Thus, Dr. Harris concludes that the data support the teaching in the present application that the compounds described therein are useful for treating bipolar disorder. See ¶26 of Declaration.

Thus, contrary to the allegations in the Office Action, the present application enables the use of the compounds described therein for the treatment of bipolar disorder. Moreover, the data submitted herewith in the Declaration support the allegations in the application that the compounds of the present invention have the alleged utility claimed herein.

Thus, for the reasons given hereinabove, the rejection of Claims 35, 36, 40-49, 57, and 68-84 under 35 U.S.C. §112, first paragraph is obviated; withdrawal thereof is respectfully requested.

Pursuant to the rejection of Claims 35, 36, 40-49, 57 and 68-84 in the Office Action alleges that the claimed subject matter is indefinite. It cites two grounds in support of its rejection.

First, it alleges that Claims 40 and 43 are unclear in that they are not subgeneric to Claim 35 upon which they depend since they do not appear to limit the definition of EWG/EDG.

Applicant disagrees. Since Claims 40-43 are ultimately dependent upon Claim 35 which defines the term "EWGs" and "EDGs", it is apparent that the terms "EWGs" and "EDGs", which appear therein, were referring to the definitions thereof in Claim 35. Nevertheless, to further emphasize that the meaning of these terms in the dependent claim is the same as in Claim 35, applicant has amended Claims 40-43 by inserting the term "said" before the terms "EWG" and "EDG", in accordance with the Examiner Lukton's suggestion during the telephone interview. Such amendment does not narrow the scope of the subject matter in Claims 40-43. However, as amended, the claim recites more explicitly that the terms "EWG" and "EDG" therein refer to the definitions recited in Claim 35.

No new matter has been added to the application.

Consequently, the rejection of Claims 40-43 under 35 USC §112, second paragraph, is obviated; withdrawal thereof is requested.

Pursuant to the second ground of the rejection of Claims 35, 36, 40-49, 57 and 68-84, the Office Action alleges that "treatment of bipolar disorder" is indefinite.

Applicant disagrees. First, bipolar disorder is defined as a form of mood disorder characterized by a variation of mood between a phase of manic or hypomanic elation, hyperactivity, and hyperimagination, and a depressive phase of inhibition, slowness to conceive ideas and move, and anxiety or sadness.

Bipolar disorder is broadly treated by the class of drugs known as mood stabilizers, which are used to prevent or mitigate all disease symptoms. It is a term of art that is readily understood by one of ordinary skill in the art. As evidence thereof, attention is directed to U.S. Patent No. 6,117,890 and specifically Column 2, Lines 49 et seq which defines the term Bipolar Disorder in accordance with standards promulgated by the American Psychiatric Association in the DSM-IV-TR.

Moreover, the metes and bounds of "treatment" of bipolar disorder are also understood by one of ordinary skill in the art. As defined on Page 48, lines 24-27, of the instant specification, the term "treat" refers to alleviating the patient's disease or condition. The use of the term "treatment of bipolar disorder" is well defined in the art. For example, attention is directed to the Claims in U.S. Patent Nos. 5,585,118 and 6,022,877, which claim a method of treating bipolar disorders. See also the claims in U.S. Patent Nos. 5,817,656 and 6,117,890. These are just four examples of patents that have issued directed to the treatment of bipolar disorder. If the United States Patent and Trademark Office issued patents directed to the treatment of bipolar disorder, it is implicitly indicating that the term "treatment of bipolar disorder" is understood by one of ordinary skill in the art. Is the Office Action now suggesting that patents which have issued from the United States Patent and Trademark Office directed to the treatment of bipolar disorder do not comply with 35 U.S.C. §112, second paragraph and that it made a mistake in issuing these patents?

The United States Patent and Trademark Office is questioning whether a drug useful for treating depression or mania alone would also be considered useful for treating bipolar disorder. Antidepressant drugs only have a potential benefit, at best, for treating the depressive symptoms that occur to varying degrees in bipolar patients. Similarly, antimanic drugs only have

a potential benefit, at best, for treating the manic symptoms that occur to varying degrees in bipolar patients. As treatment of bipolar disorder is used in the present invention, antidepressant or antimanic drugs alone do not fully treat nor are they intended to fully treat the change in moods characteristic of bipolar disorder. Such treatment for bipolar disorder, however, is one of the utilities for the compounds claimed in this application.

Thus, contrary to the allegations in the Office Action the term "treat bipolar disorder" is understood by one of ordinary skill in the art.

Therefore, for the reasons presented herein, the rejection of Claims 35, 36, 40-49, 57, and 68-84 under 35 U.S.C. §112, second paragraph, is obviated. Withdrawal thereof is respectfully requested.

In support of the rejection of Claims 35, 36, 40-49, 57 and 68-84 under 35 U.S.C. §103, the Office Action cites Kohn et al. in view of Post et al., Yang, et al. or Keck, et al.

Applicant agrees with the Office Action that Kohn et al disclose the compounds which are being utilized in the claimed subject matter. Moreover, as indicated in the Office Action, Kohn et al. disclose that these compounds are anticonvulsants. However, there is no teaching or suggestion therein that these compounds can be used to treat bipolar disorder. The Office Action concurs.

The Office Action, however, alleges that the secondary references disclose that anticonvulsants can be used to treat bipolar disorder. In other words, the Office Action is alleging that since the compounds of the present invention are anticonvulsants and since various anticonvulsants have been used to treat bipolar disorder, it would be obvious to use the compounds of the present invention to treat bipolar disorder based on the mere fact that these compounds are anticonvulsants.

Applicant respectfully submits that the United States patent and Trademark Office has not made out a prima facie case of obviousness, Case law has held that where the claimed subject matter has been rejected as obvious in view of the combination of prior art references, a proper analysis under 35 U.S.C. §103 requires, inter alia, consideration of two factors: (1) whether the prior art would have suggested to those of ordinary skill in the art that they should make the claimed composition or device or carry out the claimed process and (2) whether the prior art would also have revealed that in so making or carrying out, those of ordinary skill would have a reasonable expectation of success. In re Vaeck, 20 USPQ 1438, 1442 (Fed. Cir. 1991).

As indicated hereinabove, the primary reference discloses the compounds utilized in the present invention. However, the primary reference does not teach, disclose or suggest that the compounds recited in the instant claims are useful for treating bipolar disorder. Although the secondary references provide examples of drugs that have been useful for treating bipolar disorder, none of the drugs cited therein are subgeneric to the compounds of the present invention. In fact, none of the compounds disclosed therein are structurally related to the compounds utilized in the present invention. More specifically, Keck et al. disclose the use of valproic acid, clonazepam and carbamazepine for the treatment of bipolar disorder. Yang et al. disclose carbamazepine and lithium for treating bipolar disorders, while Post et al. disclose carbamazepine, valproic acid, benzodiazepines, such as clonazepam and lorazepam, and calcium channel blockers, such as verapamil and nimodipine. However, none of these compounds are structurally similar to or fall within the scope of the compounds described in the present invention.

Thus, the primary and secondary references taken together do not suggest that the compounds of the present invention would be useful for treating bipolar disorder.

Nevertheless, the Office Action is citing these secondary references, alleging that they teach that anticonvulsants in general are useful for treating bipolar disorder. However, the secondary references do not support the Office Action's allegations and they question whether some anticonvulsants are indeed useful for treating bipolar disorder. For example, attention is directed to Post et al., Pages 122-123, which indicate that "the primary antimanic efficacy of the benzodiazepines are difficult to assess." Page 123.

Moreover, applicant brought to the attention another drug which is anticonvulsant but which is not useful in treating bipolar disorder.

Attention in this vein is again directed to a review article entitled, "Anticonvulsants in Bipolar Disorders", by Singh et al., in Psychiatr Clin N. Am. 2005, 28, 301-323 ("Singh et al."). Gabapentin ("GBP") is a known anticonvulsant. However, attention is directed to page 315 thereof. It describes the results of experiments conducted comparing the effect of gabapentin with a placebo in a double blind, placebo controlled study on bipolar patients. This study and conclusions thereof were reported in References 59 and 60 therein which were published in 1998 and 2000, which are prior to the effective filing date of the present invention. As shown by these papers and reported by Singh et al., GBP has little or no specific effect in bipolar disorder. Thus, the authors do not recommend the use of GBP as monotherapy in the long term treatment of bipolar disorder. Moreover, as concluded on Page 320, "there is consensus" [among scientists] that some anticonvulsants "have little or no specific effect in bipolar disorder".

Thus, inasmuch as these are several examples of anticonvulsants which are not useful for treating bipolar disorder, there is no reasonable expectation of success by one of ordinary skill in the art that the mere quality of a drug being an anticonvulsant is sufficient to conclude that it would be useful for treating bipolar disorder. In fact, the Office Action so admits. Attention is directed to page 4 of the Office Action, wherein the Office Action in characterizing the compounds described in the present application as analgesics, states,

> "At this stage, the most important point is to observe that the state of the art is such the skilled psychiatrist or neurologist would have no reason to expect that compounds which induce analgesia will be effective to treat bipolar disorder."

Consequently, based therein there is no expectation of success, a priori, that the mere quality of being an anticonvulsant is sufficient to suggest that such a drug would be useful for treating bipolar disorder. Thus, since there is no expectation of success by one of ordinary skill in the art that anticonvulsant necessarily would be useful for treating bipolar disorder, there is no expectation of success based upon the prior art that the compounds of the present invention would be useful for treating bipolar disorder. In accordance with the holding in In re Vaeck, supra, the United States Patent and Trademark Office has not made a prima facie case of obviousness.

Thus, one cannot conclude that a compound which is characterized as an anticonvulsant can also be used to treat bipolar disorder. At best, it could be said that it would be obvious to try to use an anticonvulsant for treating bipolar disorder, but as the courts have held, obvious to try is not the proper standard under §103. In re Geiger, 815 F2d 686, 688, 2 USPQ 2d 1276, 1278 (Fed. Cir 1987).

The Office Action, however, alleges that the rejection is "imposed from the perspective of one who is unaware of the Singh reference or who is undeterred by its teaching".

However, this is contrary to case law. Case law has held that one of ordinary skill is one who is aware of all of the prior art. As stated in the Standard Oil Company v. American Cyanamid Co., 774 F2d 448, 227 USPQ 293 (Fed. Cir. 1985): "The issue of obvious is determined entirely with reference to a hypothetical person having ordinary skill in the art. It is only that hypothetical person who is presumed to be aware of the pertinent prior art". Id 744 F2d at 454. Thus, contrary to the allegations of the Office Action, one of ordinary skill in the art cannot ignore the teachings of the underlying papers discussed in Singh et al., which disclose that gabapentin, an anticonvulsant is not useful for treating bipolar disorder. Moreover, even if one ignored the teachings in the Singh reference, as suggested by the Office Action, one cannot ignore the teachings and suggestions in Post et al., as described hereinabove, which also show that some other anticonvulsants may not be useful in treating bipolar disorder.

Furthermore, case law has held that, in holding an invention obvious in view of a combination of references, there must be some suggestion, motivation or teaching in the prior art that would have led a person of ordinary skill in the art to select the references and combine them in a way that would produce the claimed invention. Karsten Mfg Corp v Cleveland Golf Co, 242 F3d 1376, 1385, 58 USPQ 2d 1286, 1293 (Fed. Cir. 2001). See, C.R. Bard, Inc v M3 Systems, Inc., 157 F3d 1340, 1352, 48 USPQ 2d 1225, 1232 (Fed. Cir. 1998) (a showing of a suggestion, teaching, or motivation to combine the prior art references an essential evidentiary component of an obviousness holding).

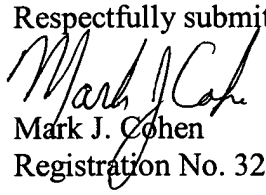
The primary reference teaches compounds utilized in the present invention as anticonvulsants, but it does not teach, disclose or suggest that they would be useful for treating bipolar disorder -- a conclusion with which the United States Patent and Trademark Office concurs. The secondary references disclose specific compounds which are useful for the

treatment of bipolar disorder, but none of them are structurally related to the compounds of the present invention. Although some of these compounds which are used to treat bipolar disorder may be anticonvulsants, there is no teaching or suggestion therein that merely because a compound is an anticonvulsant, it can be used to treat bipolar disorder. This is the teaching that is lacking in the secondary references. Without such a teaching, there is no motivation to combine the references in the manner suggested by the United States Patent and Trademark Office and the references cannot be combined in the manner suggested by the United States Patent and Trademark Office. And in fact, as suggested by the references of record, one cannot make such a conclusion as there are several anticonvulsants that are not useful for treating bipolar disorder.

Thus, for the reasons given, the rejection of Claims 35, 36, 40-49, 57 and 68-84 under 35 USC §103 is obviated, withdrawal thereof is respectfully requested.

Thus, in view of the Amendments to the Claims, the Declaration of Dr. Robert Harris, and the Remarks herein, it is respectfully submitted that the present case is in condition for allowance, which action is earnestly solicited.

Respectfully submitted,



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